REMARKS

Claims 1-3 and 5-14 are pending. No amendments have been made by way of the present submission, thus, no new matter has been added. Additionally, no new issues have been raised by way of the present submission which would require additional search and/or consideration on the part of the Examiner. In the event that the present submission does not place the application into condition for allowance, entry thereof is respectfully requested as placing the application into better condition for appeal.

In view of the following remarks Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Improper Finality of Outstanding Office Action

Applicants respectfully submit that the Finality of the outstanding Office Action is improper. In the outstanding Office Action at page 6, the Examiner has stated that the Applicant's amendment necessitated the new grounds of rejection. However, Applicants submit that the new grounds of rejection could have been made in a previous Office Action, since some of the newly rejected claims were not previously amended. Applicants note that the Examiner has rejected claims 3, 7 and 12 for the first time over the Riley reference; however, Applicants only amended claim 1 (upon which claims 3, 7 and 12 do not depend) in the

previous response. Also, the Examiner has rejected claims 5, 6 and 8-11 for the first time over Riley in view of Kaufmann however, Applicants only amended claim 1 (upon which claims 5, 6 and 8-11 do not depend) in the previous response. This is improper in view of MPEP § 706.07(a).

Accordingly, the Examiner is respectfully requested to withdraw the finality of the outstanding Office Action.

Issues Under 35 U.S.C. §102(b)

The Examiner has rejected claims 3, 7, 12 and 14 under 35 U.S.C. § 102(b) as being anticipated by Riley et al., Nucleic Acids Res., Vol. 18, No. 10, pp. 2887-2890, 1990 (herein referred to as Riley). Applicants respectfully traverse this rejection.

The Riley reference discloses restriction enzyme digestion of DNA into fragments to obtain single stranded cohesive ends and then complementary ligation of these fragments to vectorette linker adapters via complementary cohesive ends. However, this differs from the presently claimed subject matter. Claim 3 (upon which claims 7, 12 and 14 depend) requires the use of hairpin loop adapters. Hairpin loop adapters are distinct from vectorette adapters. Applicants submit that the Examiner has incorrectly characterized the "vectorette" linker adapters of Riley as being "hairpin" loop adapters required by the present claims.

The duplex vectorette of Riley unit is composed of a

combination of two single strands which have a mutually uncomplimentary region, and it is the downstream strand (which lacks 5'-cohesive NNNN) that is used in amplification. The reason of having the uncomplimentary region in this vectorette structure is so that the amplification will occur not by using a single primer of uncomplimentary region, but rather by using the primer of the uncomplimentary region in the downstream strand of the vectorette unit and the primer of base sequence of the YAC vector. In this way, only the region that comprises the vector can be amplified, and the region can be sequenced by the universal sequencing primer in the vectorette unit.

In contrast, the hairpin adaptor sequence of the present invention is a single strand adapter, not a double strand adapter, and is designed to have hairpin adaptor structure having complimentary and uncomplimentary regions by intramolecular hybridization. The uncomplimentary region is a single chain that is designed to have a stable hairpin loop structure. This is totally different is structure and use than a vectorette adaptor.

Moreover, the number of bases protruding at 5'-end in the hairpin adaptor structure of the present invention is two, while that of the vectorette of Riley is four. The protruding bases are designed to increase the variety by combination of both ends.

Accordingly, due to the differences between the hairpin loop adaptors according to the present invention as claimed and the vectorette linker adaptors of Riley, no anticipation exists.

Reconsideration and withdrawal of this rejection are respectfully requested.

Issues Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1, 5, 6, 8-11 and 13 under 35 U.S.C. § 103(a) as being obvious over Riley in view of Kaufman et al, USP 6,383,754 (herein referred to as Kaufman). Applicants respectfully traverse this rejection.

As discussed above, the hairpin loop adaptors according to the present claims (including claim 1) are distinct from the vectorette adaptors disclosed by Riley. The Riley reference provides no motivation to utilize the hairpin loop adaptors according to the present invention. A review of Kaufman will reveal that the hairpin loop structure of the present invention is not disclosed, thus, Kaufman fails to cure the deficiencies of the Riley reference. Since neither reference suggests or discloses the currently claimed subject matter, no *prima* facie case of obviousness exists. Kaufman is discussed below.

Kaufman relates to a binary encoded sequence tag (BEST) method which is disclosed by Kaufman to not utilize Type IIS restriction enzymes in the first digestion (see claim 1 of Kaufmann). In contrast, according to one embodiment of the present invention, for instance claim 5, Type IIS restriction enzymes are used. Additionally, according to Kaufamn, the DNA digested by an enzyme other than a type IIS restriction enzyme is

ligated with an offset adaptor having a recognition sequence. Then, this construct is cut at the offset site from the recognition sequence by a Type IIS restriction enzyme to produce fragments of the same length. In this way, Kaufman produces binary sequence tags by ligating the adaptor-indexer of 256 types of these fragments. Next, PCR is performed by using a specific primer to the offset and indexer sequence. At this point, phosphorothioate linkage is introduced at the 3' end of the lower strand for the single strand to have resistance to the exonuclease. The single strand is detected by hybridization with a probe, not by spreading out on a gel.

The offset adaptor and adaptor-indexer disclosed by Kaufman are double stranded with a sticky end. This is a fundamentally different structure from the hairpin loop adaptor of the present invention. Kaufman ultimately produces a binary sequence tag set having a defined length by introducing the offset cleavage site as a target DNA sequence. In the present invention, the uniqueness of treating the exonuclease is to remove the DNA sequence fragments which have not participated in the ligation by the 5'-end protruding base which follows the ligation process. This differs completely from the technology disclosed by Kaufman in which an anti-nuclease backbone is produced in the amplification process to form a single strand for hybridization.

In summary, Kaufman is unable to cure the deficiencies of the primary reference of Riley. Accordingly, when these

references are taken as a whole, the present claimed subject matter is patentably distinct. Reconsideration and withdrawal of this rejection are respectfully requested.

Information Disclosure Statement

On September 4, 2001 Applicants submitted an Information Disclosure Statement which listed three references on an attached Form PTO-1449. In the Office Action dated February 27, 2002, the Examiner indicated that this Information Disclosure Statement had been entered. However, the Examiner has not returned an fully initialed version of the September 4, 2001 Form PTO-1449 indicating that the cited references have been considered. Applicants understand that the Degau et al., USP 5,508,169 reference was acknowledged by the Examiner in the PTO-892 attached to the February 27, 2002 Office Action. Additionally, Applicants further understand that the Examiner has indicated the Guilfoyle et al., USP 5,994,068 references being considered due to its citation on the PTO-892 attached to the November 6, 2002 Amendment. However, Applicants respectfully submit that the Examiner has not yet indicated on the record that the Guilfoyle et al., USP 6,228,999 reference which was cited on the September 4, 2001 Form PTO-1449 has been considered. The Examiner is therefore respectfully requested to return a correctly initialed version of this Form PTO-1449 indicating that this reference has been considered.

In view of the above, Applicants respectfully submit that the present claims are in condition for allowance. Reconsideration and withdrawal of all rejections are respectfully requested.

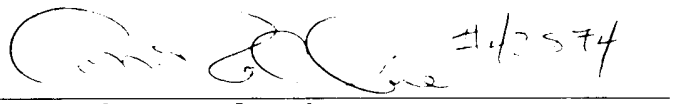
If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No. 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to August 17, 2003 in which to file a reply to the Office Action. The required fee of $110.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By  41,574

Joseph A. Kolasch
Reg. No. 22,643

JAK/CAM/gh

P. O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000